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## Doxycycline Significantly Enhances Induction of Induced Pluripotent Stem Cells to Endoderm by Enhancing Survival Through Protein Kinase B Phosphorylation.

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### Public Summary:

**BACKGROUND AND AIMS:** Induced pluripotent stem cells (iPSCs) provide an important tool for the generation of patient-derived cells, including hepatocyte-like cells, by developmental cues through an endoderm intermediate. However, most iPSC lines fail to differentiate into endoderm, with induction resulting in apoptosis. **APPROACH AND RESULTS:** To address this issue, we built upon published methods to develop an improved protocol. We discovered that doxycycline dramatically enhances the efficiency of iPSCs to endoderm differentiation by inhibiting apoptosis and promoting proliferation through the protein kinase B pathway. We tested this protocol in >70 iPSC lines, 90% of which consistently formed complete sheets of endoderm. Endoderm generated by our method achieves similar transcriptomic profiles, expression of endoderm protein markers, and the ability to be further differentiated to downstream lineages. **CONCLUSIONS:** Furthermore, this method achieves a 4-fold increase in endoderm cell number and will accelerate studies of human diseases in vitro and facilitate the expansion of iPSC-derived cells for transplantation studies.

### Scientific Abstract:

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